# WEST

## Freeform Search

**Database:** US Patents Full-Text Database; US Pre-Grant Publication Full-Text Database; JPO Abstracts Database; EPO Abstracts Database; Derwent World Patents Index; IBM Technical Disclosure Bulletins

**Term:** 11 and 12 and 13

**Display:** 20 **Documents in Display Format:** - **Starting with Number** 1

**Generate:** ○ Hit List ◉ Hit Count ○ Side by Side ○ Image

Search | Clear | Help | Logout | Interrupt

Main Menu | Show S Numbers | Edit S Numbers | Preferences | Cases

### Search History

**DATE: Thursday, May 15, 2003** Printable Copy Create Case

| Set Name side by side | Query | Hit Count | Set Name result set |
|---|---|---|---|
| *DB=USPT,PGPB; PLUR=YES; OP=AND* | | | |
| L4 | l1 and l2 and l3 | 6 | L4 |
| L3 | mg adj kg or g adj kg | 73784 | L3 |
| L2 | metastases | 12836 | L2 |
| L1 | wr-2721 | 99 | L1 |

END OF SEARCH HISTORY

Generate Collection | Print

**Search Results** - Record(s) 1 through 6 of 6 returned.

☐ 1. 20030086924 . 10 Oct 02. 08 May 03. Treatment with anti-ErbB2 antibodies. Sliwkowski, Mark X.. 424/143.1; 424/155.1 A61K039/395.

☐ 2. 20020132795 . 03 May 02. 19 Sep 02. Methods for treatment of neuro- and nephro- disorders and therapeutic toxicities using aminothiol compounds. Stogniew, Martin, et al. 514/114; 514/625 514/646 514/665 A61K031/66 A61K031/135 A61K031/16 A61K031/13.

☐ 3. 20020001587 . 16 Mar 01. 03 Jan 02. Methods of treatment using anti-ErbB antibody-maytansinoid conjugates. Erickson, Sharon, et al. 424/178.1; A61K039/395.

☐ 4. 6495129 . 13 Oct 00; 17 Dec 02. Methods of inhibiting hematopoietic stem cells using human myeloid progenitor inhibitory factor-1 (MPIF-1) (Ckbeta-8/MIP-3). Li; Haodong, et al. 424/85.1; 514/12 514/2 514/8. A61K038/19.

☐ 5. 6426366 . 07 Apr 99; 30 Jul 02. Pharmaceutical compositions comprising tyrphostins. Novogrodsky; Abraham, et al. 514/523; 514/525. G61K031/275.

☐ 6. 5994409 . 09 Dec 97; 30 Nov 99. Methods for treatment of neuro--and nephro--disorders and therapeutic toxicities using aminothiol compounds. Stogniew; Martin, et al. 514/665; 514/114 514/649. A01N038/08 A01N057/00 A01N033/02.

Generate Collection | Print

| Terms | Documents |
|---|---|
| l1 and l2 and l3 | 6 |

Previous Page Next Page

=> d his

(FILE 'HOME' ENTERED AT 17:10:46 ON 15 MAY 2003)

FILE 'MEDLINE, CAPLUS, BIOSIS, SCISEARCH' ENTERED AT 17:11:01 ON 15 MAY 2003

L1 2610 S WR-2721
L2 27 S METASTASES AND L1
L3 0 S MG/KG OR G/KG
L4 840460 S MG(W)KG OR G(W)KG
L5 9 S L2 AND L4
L6 5 DUP REM L5 (4 DUPLICATES REMOVED)

=> d bib ab 1-5 l6

L6 ANSWER 1 OF 5 SCISEARCH COPYRIGHT 2003 THOMSON ISI
AN 2002:19970 SCISEARCH
GA The Genuine Article (R) Number: 504WB
TI Inhibition of spontaneous **metastases** formation by amifostine
AU Grdina D J (Reprint); Kataoka Y; Murley J S; Hunter N; Weichselbaum R R; Milas L
CS Univ Chicago, Dept Radiat & Cellular Oncol, MC1105, Rm E-SB-11B, 5841 S Maryland Ave, Chicago, IL 60637 USA (Reprint); Univ Chicago, Dept Radiat & Cellular Oncol, Chicago, IL 60637 USA; Univ Texas, MD Anderson Canc Ctr, Dept Expt Radiat Oncol, Houston, TX 77030 USA
CYA USA
SO INTERNATIONAL JOURNAL OF CANCER, (10 JAN 2002) Vol. 97, No. 2, pp. 135-141.
Publisher: WILEY-LISS, DIV JOHN WILEY & SONS INC, 605 THIRD AVE, NEW YORK, NY 10158-0012 USA.
ISSN: 0020-7136.
DT Article; Journal
LA English
REC Reference Count: 36
*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS*
AB Amifostine was investigated for its ability to inhibit spontaneous **metastases** formation using the well-characterized murine sarcoma, Sa-NH. Amifostine was administered intraperitoneally at a dose of 50 **mg/kg** every other day for 6 days to C3Hf/Kam mice until tumors reached an average size of 8-8.5 mm in diameter. Amifostine was again administered immediately after surgical removal of the tumor-bearing limbs by amputation, and then once more 2 days later. Twenty-one days later, animals were evaluated for the presence of spontaneously developed pulmonary **metastases**. Nontumor-bearing control animals were sham treated using the same dosing and surgery schedules. Treatment with amifostine appeared to slightly delay tumor growth, that is, 13 vs. 12 days for tumors to reach an average diameter of 8 mm. Amifostine reduced both the incidence of pulmonary **metastases** formed in experimental animals from 77% to 57% (p<0.05), and their average number per animal from 12.8<plus/minus>5.4 (SEM) to 2.9 +/-1.1 (SEM). The effect of amifostine exposure on serum levels of the angiogenesis inhibitor angiostatin was also determined using Western blot analysis. Consistent with the antimetastatic effect, exposure of animals to 50 **mg/kg** of amifostine resulted in a 4-fold enhanced serum level of angiostatin above control levels. This phenomenon occurred in tumor-bearing and nontumor-bearing animals. The effects of amifostine on matrix metalloproteinase (MMP) enzymatic activity was also determined using gelatin zymography. Conditioned growth medium collected from Sa-NH cells grown to confluency was exposed to various concentrations of SH, i.e., 2-[(aminopropyl)amino]ethane-thiol (WR-1065), the active thiol form of amifostine, for either 30 min or 18 hr. WR-1065, as a function of increasing dose and time, inhibited the enzymatic activities of MMP-2 and MMP-9. At a concentration and time of exposure likely to be achieved in

vivo, that is, 40 muM and 30 min, MMP-2 and MMP-9 activities were reduced to between 30% and 40% of control values. Consistent with these affects, WR-1065 was also found to be effective in inhibiting the ability of Sa-NH cells to migrate through Matrigel membranes. After an 18-hr exposure under in vitro conditions, WR-1065 at concentrations of 4, 40 and 400 muM, and 4 mM, inhibited Sa-NH migration to 11%, 44%, 81% and 97% of control values, respectively. The abilities of amifostine and its active thiol WR-1065 to stimulate angiostatin production in mice, and to inhibit the MMP enzymatic activities and invasion ability of Sa-NH cells under in vitro conditions, are consistent with the observed antimetastatic effects exhibited against Sa-NH tumors growing in vivo. (C) 2002 Wiley-Liss, Inc.

L6 ANSWER 2 OF 5 MEDLINE DUPLICATE 1
AN 88114786 MEDLINE
DN 88114786 PubMed ID: 2828290
TI Influence of misonidazole, SR-2508, RSU-1069 and **WR-2721** on spontaneous **metastases** in C57BL mice.
AU Kanclerz A; Chapman J D
CS Department of Radiation Oncology, Cross Cancer Institute, University of Alberta, Edmonton, Canada.
SO INTERNATIONAL JOURNAL OF RADIATION ONCOLOGY, BIOLOGY, PHYSICS, (1988 Feb) 14 (2) 309-16.
Journal code: 7603616. ISSN: 0360-3016.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198803
ED Entered STN: 19900308
Last Updated on STN: 19900308
Entered Medline: 19880310
AB The effect of treatments with the hypoxic cell radiosensitizers misonidazole (MISO), SR-2508, RSU-1069, and with the radioprotector **WR-2721** on spontaneously disseminated Lewis lung carcinoma (LLC) and B16 melanoma (B16M) was investigated. Tumors were implanted into the tails of C57BL mice and were surgically removed after reaching volumes of approximately 40 mm3. This technique results in the induction of metastatic disease in lungs and at other anatomical sites and allows the independent treatment of disseminated tumor cells. The radiosensitizers and the radioprotector were administered 24 hr after surgery and animals were killed 14 and 30 days after removal of LLC and B16M, respectively. The time to death from spontaneous **metastases** was also measured. Both single treatments with large doses of MISO (1.0 **g/kg**) and fractionated therapy with smaller doses (0.5 **g/kg** on 5 consecutive days) promoted the formation of **metastases** to the lungs, lymph nodes and other organs. The survival times of MISO treated animals did not differ from control animals but manifestation of metastatic disease in the lungs and other organs occurred at earlier times. Administration of equitoxic doses of SR-2508 (3.0 **g/kg**) and RSU-1069 (0.1 **g/kg**) also promoted **metastases** formation. Mice treated with these radiosensitizers developed more **metastases** in the lungs and at other sites. Treatment with a single dose of **WR-2721** (0.4 **g/kg**) promoted lung **metastases** but exerted a suppressive effect on lymph node tumors. When the radioprotector was given in fractionated schedules in three different doses (0.05 **g/kg**, 0.1 **g/kg** and 0.2 **g/kg** for 10 consecutive days) a slight enhancement of lung **metastases** and suppression of extrapulmonary **metastases** was observed.

L6 ANSWER 3 OF 5 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 1984:324712 BIOSIS
DN BA78:61192

TI PROTECTION BY S-2-3 AMINOPROPYLAMINOETHYLPHOSPHOROTHIOIC-ACID AGAINST RADIATION INDUCED AND CYCLO PHOSPHAMIDE INDUCED ATTENUATION IN ANTI TUMOR RESISTANCE.

AU MILAS L; MCBRIDE W H; HUNTER N; ITO H
CS DEP. EXPERIMENTAL RADIOTHERAPY, UNIV. TEX. M. D. ANDERSON HOSPITAL TUMOR INST., HOUSTON, TX 77030.

SO CANCER RES, (1984) 44 (6), 2382-2386.
CODEN: CNREA8. ISSN: 0008-5472.
FS BA; OLD
LA English

AB Studies were performed to investigate whether S-2-(3-aminopropylamino)ethylphosphorothioic acid (**WR-2721**) can protect antitumor immune rejection responses against the damaging effects of whole-body irradiation (WBI) and cyclophosphamide (CY). Among these damaging effects were radiation-induced enhancement of s.c. tumor take and radiation- and CY-induced enhancement of lung colonization by tumor cells injected i.v. The ability of **WR-2721** to protect against WBI-induced decreased radio response of solitary tumors was also investigated. All experiments were performed with an immunogenic fibrosarcoma syngeneic to C3Hf/Kam mice. **WR-2721** was given i.p. at a dose of 400 **mg/kg** 30 min before WBI with .gamma.-rays or CY injection. WBI with 650 rads reduced the number of tumor cells needed for tumor take in 50% of animals from 5.1 .times. 104 cells in normal mice to 2.0 .times. 102. **WR-2721** given before WBI almost entirely abolished the effect of WBI: the number of tumor cells needed for tumor take in 50% of animals was 1.4 .times. 104. Treatment of mice with WBI or CY increased the number of tumor nodules in the lung generated by fibrosarcoma cells injected i.v. 5 days later, in a linear dose response. **WR-2721** greatly reduced this metastasis enhancement effect of WBI and CY with protection factors of 2.5 for WBI and 1.8 for CY. Fibrosarcomas of 8 mm in diameter exhibited a decreased radiocurability when growing in WBI mice: the dose of irradiation yielding local tumor control in 50% of animals in these mice was 5950 compared to a dose of irradiation yielding local tumor control in 50% of animals of 4160 rads in normal mice. **WR-2721** given before WBI inhibited this effect of WBI: the dose of irradiation yielding local tumor control in 50% of animals was 5210 rads. The proportion of macrophages in tumors growing in WBI mice was significantly reduced, but not when **WR-2721** was first given. **WR-2721** greatly reduced the damaging effects of WBI and CY on natural killer cell activity. Therefore, **WR-2721** was capable of protecting the immune mechanisms involved in antitumor resistance against WBI and CY. This might be of therapeutic benefit when **WR-2721** is combined with radio- or chemotherapy.

L6 ANSWER 4 OF 5 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 1984:292580 BIOSIS
DN BA78:29060
TI EFFECT OF TUMOR TYPE SIZE AND END POINT ON TUMOR RADIOPROTECTION BY **WR-2721** S-2-3 AMINOPROPYLAMINO ETHYL PHOSPHOROTHIOIC-ACID.

AU MILAS L; HUNTER N; ITO H; PETERS L J
CS DEPARTMENT OF EXPERIMENTAL RADIOTHERAPY, M.D. ANDERSON HOSPITAL, 6723 BERTNER AVE., HOUSTON, TEXAS 77030.

SO INT J RADIAT ONCOL BIOL PHYS, (1984) 10 (1), 41-48.
CODEN: IOBPD3. ISSN: 0360-3016.
FS BA; OLD
LA English

AB Experiments are reported showing that the degree of tumor radioprotection afforded by **WR-2721** (S-2-(3-aminopropylamino)-ethylphosphorothioic acid) varies with the type of tumor and assay endpoint, and that for a given tumor system, microaggregates are protected better than larger cell masses. The tumor used were a methylcholanthrene[carcinogen]-induced fibrosarcoma [murine] (FSa), and 2

tumors of spontaneous origin, another fibrosarcoma (NFSa), and a mammary carcinoma (MCa-4), all syngeneic to C3Hf/Kam mice. **WR-2721** was given in a dose of 400 **mg/kg** 30 min before irradiation in all experiments. In TCD50 assays, **WR-2721** protected 5 nm diameter and impalpable 3 day old transplant of 5 .times. 105 FSa cells growing in the leg by factors of 1.11 and 1.13, respectively. Using the tumor latency endpoint, 3 day-old s.c. transplants of 103 FSa in the abdominal wall were protected by a factor of 1.27, a degree of protection similar to that reported earlier for sterilization of lung micrometastases of the same tumor. MCa-4 tumors growing in the leg were protected better than FSa in TCD50 assays with protection factors of 1.3 for 4 day old transplants, 1.24 for 5 mm tumors, and 1.23 for 8 mm tumors. MCa-4 tumors recurrent after irradiation as 4 day old transplants grew more rapidly in mice that received **WR-2721**, and this was shown to be most likely due to protection by the drug against expression of the tumor bed effect. Using the lung micrometastases assay, NFSa was protected by a factor of 1.22. This variability in protection with different tumor types, sizes and assay endpoints is discussed in terms of drug delivery and uptake, and also in relation to the influence of tumor hypoxia on the radioprotective ability of **WR-2721**.

L6 ANSWER 5 OF 5 MEDLINE DUPLICATE 2
AN 83206571 MEDLINE
DN 83206571 PubMed ID: 6303574
TI Effect of tumor size on S-2-(3-aminopropylamino)ethylphosphorothioic acid and misonidazole alteration of tumor response to cyclophosphamide.
AU Milas L; Ito H; Hunter N
NC CA-06294 (NCI)
SO CANCER RESEARCH, (1983 Jul) 43 (7) 3050-6.
Journal code: 2984705R. ISSN: 0008-5472.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198307
ED Entered STN: 19900319
Last Updated on STN: 19970203
Entered Medline: 19830729
AB The influence of tumor size on the ability of S-2-(3-aminopropylamino)ethylphosphorothioic acid (**WR-2721**) or misonidazole (MISO) to alter cyclophosphamide (CY) antitumor activity was investigated, using a chemically induced fibrosarcoma (FSA) and a spontaneous fibrosarcoma (NFSA) in C3Hf/Kam mice. Tumors were of two sizes at the time of treatment, 8-mm leg tumors and 4-day-old micrometastases in the lung. The antitumor activity of CY and its modification were assessed by growth delay of leg tumors and the reduction in the number of lung **metastases**. Both measures of tumor response were more pronounced as the dose of CY increased, and FSA was more sensitive to CY than was NFSA. **WR-2721** (400 **mg/kg**), given 30 min before treatment with CY, reduced the effectiveness of CY on both FSA and NFSA. This reduction in effectiveness of CY was only minimal for leg tumors (dose-modifying factors were 1.1 for FSA and 1.03 for NFSA) but remarkable for lung micrometastases (dose-modifying factors were 1.81 for FSA and 1.55 for NFSA). Protection increased with the increase in the dose of **WR-2721** and was also dependent on the time of injection relative to CY. The greatest protection occurred when **WR-2721** was given within 30 min before to 15 min after CY. Tumor size had the opposite effect on MISO from that on **WR-2721**. MISO (1 mg/g) enhanced the effect of CY more effectively for leg tumors than for lung micrometastases: dose-modifying factors were 1.74 for FSA and 2.21 for NFSA growing in the leg and 1.27 for FSA and 1.11 for NFSA lung micrometastases. Therefore, tumor size appears to be a very important

factor in determining the extent of WR-2721- and MISO-induced modification of CY antitumor effect.

=>

=> d his

(FILE 'HOME' ENTERED AT 11:30:51 ON 15 MAY 2003)

FILE 'MEDLINE, CAPLUS, BIOSIS, SCISEARCH' ENTERED AT 11:31:01 ON 15 MAY 2003

L1 3344 S WR(W)(2721 OR 1065 OR 638 OR 77913 OR 33278 OR 3689 OR 2822 O
L2 29241 S (DIFFICULT? OR PROBLEM OR PITFALL OR DRAWBACK)(8A)(CANCER OR
L3 6 S L1 AND L2
L4 3 DUP REM L3 (3 DUPLICATES REMOVED)

=> d bib ab 1-3 l4

L4 ANSWER 1 OF 3 MEDLINE DUPLICATE 1
AN 2001294068 MEDLINE
DN 21271445 PubMed ID: 11379297
TI Amifostine (Ethyol) as modulator of hepatic and biliary toxicity from intraarterial hepatic chemoembolization: results of a phase I study.
AU Fiorentini G; Giovanis P; Leoni M; De Giorgi U; Cariello A; Dazzi C; Caldeo A
CS Oncology Department, City Hospital, v.le Randi 5, Ravenna 48100, Italy.. oncologia@ra.nettuno.it
SO HEPATO-GASTROENTEROLOGY, (2001 Mar-Apr) 48 (38) 313-6.
Journal code: 8007849. ISSN: 0172-6390.
CY Greece
DT (CLINICAL TRIAL)
(CLINICAL TRIAL, PHASE I)
Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200110
ED Entered STN: 20011015
Last Updated on STN: 20011015
Entered Medline: 20011011
AB BACKGROUND/AIMS: Hepatic and biliary toxicity are still significant **problems** after intraarterial hepatic chemoembolization for liver **metastases** from large bowel cancers. In about 30-60% of the patients hepatic and biliary toxicity are the limiting aspects of intraarterial hepatic chemoembolization and exclude a lot of patients from a repeated beneficial treatment. Amifostine (Ethyol) is a prodrug that must be dephosphorylated to the free thiol in which form it can detoxify free oxygen radicals generated by radiation, hypoxia and by drugs such anthracyclines, platinum analogues and alkylating agents. Amifostine as inactive prodrug is primarily metabolized at the tissue site by membrane alkaline phosphatase, which is highly active in the cell membranes of normal endothelial cells and biliary tree cells but not in the cell membranes and neovascular capillaries of tumor. When dephosphorylated to **WR-1065**, amifostine is rapidly taken up into normal liver cells by a carrier-mediated facilitated diffusion transport process. The resulting high thiol content in normal liver tissue (biliary cells and hepatocytes) compared with the negligible concentration in liver metastases from large bowel cancers probably provides for selective drug resistance to intraarterial hepatic chemoembolization protecting normal tissue and allowing full therapeutic effect on tumor. METHODOLOGY: From May 1997 we planned a phase I study in patients receiving intraarterial hepatic chemoembolization for liver metastases from large bowel cancers. We started at 200 mg/m2 dissolved in 250 cc of normal saline given in 15 min in the intrahepatic artery 20 min before an intraarterial hepatic chemoembolization consisting of mitomycin 10 mg/m2, epirubicin-50, cisplatin-60 diluted in 10 mL of contrast media, mixed in 15 mL of lipiodol UF followed by a gelfoam powder solution until stagnation of the flow. The escalating dose, every 3 patients, was: 200 mg/m2, 250 mg/m2, 300 mg/m2, 350 mg/m2. RESULTS: Toxicity has been observed at 350 mg/m2: 1 patient reported transient hypotension (Blood pressure 70/50 mm Hg), 1

patient had skin flushing and dyspnoea. 300 mg/m2 are well tolerated and seem to reduce the level of transaminases, lactic acid dehydrogenase, and gamma-glutamyl transferase. Also the duration of necrotic damage, always observed after intraarterial hepatic chemoembolization, seems shorter compared with historical controls. CONCLUSIONS: Amifostine can be certainly administered at 300 mg/m2 as intraarterial infusion and could be a significant step to ameliorate the therapeutic ratio of intraarterial hepatic chemoembolization.

L4 ANSWER 2 OF 3 SCISEARCH COPYRIGHT 2003 THOMSON ISI
AN 93:210382 SCISEARCH
GA The Genuine Article (R) Number: KU669
TI COLORECTAL-CANCER - WHATS NEW IN 1992
AU RIVOIRE M (Reprint)
CS CTR LEON BERARD, DEPT CHIRURG, 28 RUE LAENNEC, F-69373 LYON, FRANCE (Reprint)
CYA FRANCE
SO PATHOLOGIE BIOLOGIE, (DEC 1992) Vol. 40, No. 9BIS, pp. 943-948. ISSN: 0369-8114.
DT Article; Journal
FS LIFE
LA French
REC Reference Count: 3
*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS*
AB Five studies presented at the 1992 ASCO meeting are analysed. Kligerman's study was designed to determine if pre-treatment with **WR-2721** could protect normal tissues from the toxicities induced by radiation therapy (in 100 patients with advanced rectal cancer). This pre-treatment resulted in a 13 % reduction of moderate and severe acute toxicity. No **WR-2721** patient experienced moderate or severe late toxicities compared to five in the group without pre-treatment. The complete response rate was higher in the **WR-2721** group and there was no major **WR-2721** related toxicity. Minski studied the acute toxicity (during treatment and two weeks after) of combined pelvic radiation therapy, 5-FU and leucovorin when delivered pre-operatively (16 patients) versus post-operatively (25 patients) in patients with rectal cancer. The toxicity criteria were fatigue, diarrhea, tenesmus, bowel movements, dysuria and erythema. Grade 3+ toxicity was more important in the post-operative therapy group (48 % versus 13 %). Given this high incidence of grade 3+ toxicity future randomized trials should explore the pre-operative approach. The final report of the inter group study of 5-FU plus levamisole as adjuvant therapy for stage C colon cancer was made by Moertel. With a median follow-up time of 5.5 years, the 5-FU plus levamisole treatment has reduced the recurrence rate by 39 %, the cancer related death rate by 32 % and the overall death rate by 31 %. Most of the recurrences occurred during the first two years. There was a decrease in the liver, great omentum, peritoneum and lung metastases, but there was no modification in loco-regional recurrence rate. Welt presented a phase I/II study of radio-immunotherapy with I-131-monoclonal antibody A33 in patients with advanced colorectal carcinoma. Results were characterised by major hematologic toxicity and minor tumor response rate. This study (from a leading research team working with one of the best monoclonal antibody) outline the extreme **difficulty** of **cancer** therapy with radio-labeled monoclonal antibody. Humanization of A33 is planned to improve these results. Heiss undertook a prospective study to evaluate the influence of homologous blood transfusion on recurrence rate after colorectal cancer surgery. Fifty-eight patients receiving autologous blood transfusion were compared with sixty-two patients receiving homologous transfusion. With a median follow-up of 21 months a higher recurrence rate was found in the homologous group (29.4 % versus 16.7 %). This study methodology is rather criticizable, but its main interest is to focus on the immunosupressive effect of blood transfusion during surgery in cancer patients.

L4 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2003 ACS
AN 1987:644616 CAPLUS
DN 107:244616
TI Chemical radioprotectors: assessment and prospects
AU Fatome, M.
CS Div. Radiobiol. Radioprot., Cent. Rech. Serv. de Sante des Armees, Clamart, 92141, Fr.
SO Radioprotection (1987), 22(3), 209-18
CODEN: RAPRBA; ISSN: 0033-8451
DT Journal; General Review
LA French
AB The best radioprotective compds. are still aminothiol derivs., the most active being the phosphorothioate **WR 2721**. In spite of clin. trials carried out in the United States with this compd. because of its low or negligible effect on **tumor** cells, their human application presents some **difficulties**, the most important coming from the risk of appearance of side-effects. An enhancing of their activity and a lowering of their toxicity have been obtained with new assocns. of compds. and, concerning the oral way, by their incorporation into carriers. Their action mechanisms is complex and multiple. Except free radical scavenging, hypoxia and glutathion peroxydase activation are certainly important factors. They have no action on the incidence of radio-induced nausea and vomiting, the prevention of which remains difficult. On the other hand, at least some of them seem to have an antimutagenic and antineoplastic effect, even if given after irradn. 35 Refs.

=>

```
=> d his

     (FILE 'HOME' ENTERED AT 13:32:15 ON 15 MAY 2003)

     FILE 'MEDLINE, CAPLUS, BIOSIS, SCISEARCH' ENTERED AT 13:32:34 ON 15 MAY
     2003
L1          2610 S WR-2721
L2         29218 S LUNG(6A)METASTAS?
L3            21 S L1 AND L2
L4            12 DUP REM L3 (9 DUPLICATES REMOVED)
L5          1818 S (REDUC? OR DIMINISH? OR DECREAS? OR INHIBIT?)(7A)LUNG(6A)META
L6          3934 S (REDUC? OR DIMINISH? OR DECREAS? OR INHIBIT?)(7A)LUNG(6A)META
L7             6 S L1 AND L6
L8             4 DUP REM L7 (2 DUPLICATES REMOVED)

=> d bib ab 1-4 l8

L8   ANSWER 1 OF 4  CAPLUS  COPYRIGHT 2003 ACS
AN   2000:688056  CAPLUS
DN   133:247270
TI   Phosphorothioates and phosphorothioate metabolites for protection against
     tumor metastasis formation
IN   Grdina, David J.; Milas, Luka
PA   Arch Development Corp., USA; Board of Regents, the University of Texas
     System
SO   PCT Int. Appl., 57 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 1
     PATENT NO.         KIND  DATE           APPLICATION NO.  DATE
     ---------------    ----  --------       ---------------  --------
PI   WO 2000056299      A2    20000928       WO 2000-US6653   20000314
     WO 2000056299      A3    20010118
         W:  AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU,
             CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL,
             IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA,
             MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI,
             SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM,
             AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,
             DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,
             CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
PRAI US 1999-125605P   P     19990319
     US 2000-523886    A1    20000313
AB   Methods and pharmaceuticals are provided for inhibiting or preventing
     metastasis formation in animals, including humans, having primary tumors,
     through the administration of phosphorothioates including their thiol and
     disulfide metabolites.  These compds. stimulate angiostatin levels,
     inhibit matrix metalloproteinases, and stimulate manganese superoxide
     dismutase.  Phosphorothioates, e.g. amifostine, can be administered as a
     combination therapy with traditional cancer therapies, including
     chemotherapy, radiotherapy, surgery, immunotherapy, hormone therapy, and
     gene therapy.  Inhibition or prevention of metastasis by phosphorothioates
     is independent of tumor type, including adenocarcinomas and sarcomas.

L8   ANSWER 2 OF 4     MEDLINE
AN   93268508     MEDLINE
DN   93268508   PubMed ID: 1338919
TI   [Cancers of the colon and the rectum: news in 1992].
     Cancers du colon et du rectum: nouveautes en 1992.
AU   Rivoire M
CS   Departement de Chirurgie, Centre Leon Berard, Lyon, France.
```

SO PATHOLOGIE BIOLOGIE, (1992 Dec) 40 (9 Pt 2) 943-8.
Journal code: 0265365. ISSN: 0369-8114.
CY France
DT News Announcement
LA French
FS Priority Journals
EM 199306
ED Entered STN: 19930702
Last Updated on STN: 19930702
Entered Medline: 19930621
AB Five studies presented at the 1992 ASCO meeting are analysed. Kligerman's study was designed to determine if pre-treatment with **WR-2721** could protect normal tissues from the toxicities induced by radiation therapy (in 100 patients with advanced rectal cancer). This pre-treatment resulted in a 13% reduction of moderate and severe acute toxicity. No **WR-2721** patient experienced moderate or severe late toxicities compared to five in the group without pre-treatment. The complete response rate was higher in the **WR-2721** group and there was no major **WR-2721** related toxicity. Minski studied the acute toxicity (during treatment and two weeks after) of combined pelvic radiation therapy, 5-FU and leucovorin when delivered pre-operatively (16 patients) versus post-operatively (25 patients) in patients with rectal cancer. The toxicity criteria were fatigue, diarrhea, tenesmus, bowel movements, dysuria and erythema. Grade 3+ toxicity was more important in the post-operative therapy group (48% versus 13%). Given this high incidence of grade 3+ toxicity future randomized trials should explore the pre-operative approach. The final report of the inter group study of 5-FU plus levamisole as adjuvant therapy for stage C colon cancer was made by Moertel. With a median follow-up time of 5.5 years, the 5-FU plus levamisole treatment has reduced the recurrence rate by 39%, the cancer related death rate by 32% and the overall death rate by 31%. Most of the recurrences occurred during the first two years. There was a **decrease** in the liver, great omentum, peritoneum and **lung metastases**, but there was no modification in loco-regional recurrence rate.(ABSTRACT TRUNCATED AT 250 WORDS)

L8 ANSWER 3 OF 4 SCISEARCH COPYRIGHT 2003 THOMSON ISI
AN 93:210382 SCISEARCH
GA The Genuine Article (R) Number: KU669
TI COLORECTAL-CANCER - WHATS NEW IN 1992
AU RIVOIRE M (Reprint)
CS CTR LEON BERARD, DEPT CHIRURG, 28 RUE LAENNEC, F-69373 LYON, FRANCE (Reprint)
CYA FRANCE
SO PATHOLOGIE BIOLOGIE, (DEC 1992) Vol. 40, No. 9BIS, pp. 943-948.
ISSN: 0369-8114.
DT Article; Journal
FS LIFE
LA French
REC Reference Count: 3
*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS*
AB Five studies presented at the 1992 ASCO meeting are analysed. Kligerman's study was designed to determine if pre-treatment with **WR-2721** could protect normal tissues from the toxicities induced by radiation therapy (in 100 patients with advanced rectal cancer). This pre-treatment resulted in a 13 % reduction of moderate and severe acute toxicity. No **WR-2721** patient experienced moderate or severe late toxicities compared to five in the group without pre-treatment. The complete response rate was higher in the **WR-2721** group and there was no major **WR-2721** related toxicity. Minski studied the acute toxicity (during treatment and two weeks after) of combined pelvic radiation therapy, 5-FU and leucovorin when delivered pre-operatively (16 patients) versus post-operatively (25

patients) in patients with rectal cancer. The toxicity criteria were fatigue, diarrhea, tenesmus, bowel movements, dysuria and erythema. Grade 3+ toxicity was more important in the post-operative therapy group (48 % versus 13 %). Given this high incidence of grade 3+ toxicity future randomized trials should explore the pre-operative approach. The final report of the inter group study of 5-FU plus levamisole as adjuvant therapy for stage C colon cancer was made by Moertel. With a median follow-up time of 5.5 years, the 5-FU plus levamisole treatment has reduced the recurrence rate by 39 %, the cancer related death rate by 32 % and the overall death rate by 31 %. Most of the recurrences occurred during the first two years. There was a **decrease** in the liver, great omentum, peritoneum and **lung metastases**, but there was no modification in loco-regional recurrence rate. Welt presented a phase I/II study of radio-immunotherapy with I-131-monoclonal antibody A33 in patients with advanced colorectal carcinoma. Results were characterised by major hematologic toxicity and minor tumor response rate. This study (from a leading research team working with one of the best monoclonal antibody) outline the extreme difficulty of cancer therapy with radio-labeled monoclonal antibody. Humanization of A33 is planned to improve these results. Heiss undertook a prospective study to evaluate the influence of homologous blood transfusion on recurrence rate after colorectal cancer surgery. Fifty-eight patients receiving autologous blood transfusion were compared with sixty-two patients receiving homologous transfusion. With a median follow-up of 21 months a higher recurrence rate was found in the homologous group (29.4 % versus 16.7 %). This study methodology is rather criticizable, but its main interest is to focus on the immunosupressive effect of blood transfusion during surgery in cancer patients.

L8 ANSWER 4 OF 4 MEDLINE DUPLICATE 1
AN 83206571 MEDLINE
DN 83206571 PubMed ID: 6303574
TI Effect of tumor size on S-2-(3-aminopropylamino)ethylphosphorothioic acid and misonidazole alteration of tumor response to cyclophosphamide.
AU Milas L; Ito H; Hunter N
NC CA-06294 (NCI)
SO CANCER RESEARCH, (1983 Jul) 43 (7) 3050-6.
Journal code: 2984705R. ISSN: 0008-5472.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198307
ED Entered STN: 19900319
Last Updated on STN: 19970203
Entered Medline: 19830729
AB The influence of tumor size on the ability of S-2-(3-aminopropylamino)ethylphosphorothioic acid (**WR-2721**) or misonidazole (MISO) to alter cyclophosphamide (CY) antitumor activity was investigated, using a chemically induced fibrosarcoma (FSA) and a spontaneous fibrosarcoma (NFSA) in C3Hf/Kam mice. Tumors were of two sizes at the time of treatment, 8-mm leg tumors and 4-day-old micrometastases in the lung. The antitumor activity of CY and its modification were assessed by growth delay of leg tumors and the **reduction** in the number of **lung metastases**. Both measures of tumor response were more pronounced as the dose of CY increased, and FSA was more sensitive to CY than was NFSA. **WR-2721** (400 mg/kg), given 30 min before treatment with CY, reduced the effectiveness of CY on both FSA and NFSA. This reduction in effectiveness of CY was only minimal for leg tumors (dose-modifying factors were 1.1 for FSA and 1.03 for NFSA) but remarkable for lung micrometastases (dose-modifying factors were 1.81 for FSA and 1.55 for NFSA). Protection increased with the increase in the dose of **WR-2721** and was also dependent on the time of injection relative

to CY. The greatest protection occurred when **WR-2721** was given within 30 min before to 15 min after CY. Tumor size had the opposite effect on MISO from that on **WR-2721**. MISO (1 mg/g) enhanced the effect of CY more effectively for leg tumors than for lung micrometastases: dose-modifying factors were 1.74 for FSA and 2.21 for NFSA growing in the leg and 1.27 for FSA and 1.11 for NFSA lung micrometastases. Therefore, tumor size appears to be a very important factor in determining the extent of **WR-2721**- and MISO-induced modification of CY antitumor effect.

=>